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09/592,695	06/13/2000	Andrea G Cochran	P1762R1	7146

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EXAMINER	
WESSENDORF, TERESA D	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 03/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/592,695	COCHRAN ET AL.	
	Examiner	Art Unit	
	T. D. Wessendorf	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 December 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,7-12 and 20-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 7-12 and 20-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

Claims 1-3, 7-12 and 20-23 are pending and under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

Claims 1-3, 7-12 and 20-23, as amended, are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention and repeated below.

To satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the genus of the invention. The specification describes a cyclic peptide wherein position A3 is of defined structure without additional amino acid of 1-50 at either or both the N or C -terminus. The disclosure states that A3 residue, as define, is necessary to modify the other residues to obtain the different beta turns, hairpin, bulge or other turns. The specification does not describe A3 with any combinations of residues of length greater than four or five residues. More

importantly, in combination with any number of residues at each or both ends of the peptide sequence. A written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula [or] chemical name of the claimed subject matter sufficient to distinguish it from other materials. University of California v. Eli Lilly and Col, 43 USPQ 2d 1398, 1405(1997), quoting Fiers V. Revel, 25 USPQ 2d 1601m 16106 (Fed. Cir. 1993). See also University of Rochester v. G.D. Searle & Co., 68 USPQ2d 1424 (DC WNY 2003). The specific amino acids for A3 in combination with the general statements with respect to the different N or C amino acids will not be a description of the huge scope of the present claims. The specification does not describe the kind, length or combination of amino acid residues in the short cyclic peptide that A3 can possess to exhibit any turns for the peptide. Likewise, there is no specific description of the cyclic peptide having the undefined residues at the N or C end. The Examples presented in the specification demonstrates how so much a change in one residue, especially for a short length peptide can result in a conformationally unstable peptide. The art is inherently unpredictable. It is not possible to predict that even with a predetermined sequence for said A3 with the N or C end the

effect of other amino acid fragments. It cannot be ascertained from the undefined structure if one can reliably predict a conformationally or properly folded peptide. It is generally known that there are still no rules that have emerged that allow structure to be related to sequence in any simple fashion (even as applied to the actual compounds). In biotechnological invention one cannot necessarily claim a genus after only describing a single species because there may be unpredictability in the results obtained from species other than those specifically described. One may not preempt an unduly large field by the expedient of making broad prophetic statements in the specification and claim unless the accuracy of such statements is sufficiently supported by well-established chemical principles or by sufficient number of examples. Applicants, at the time of filing, are deemed to have not invented species sufficient to constitute the genus by virtue of having disclosed a three species when the evidence indicates ordinary artisans could not predict the operability in the invention of any species other than the one disclosed. In re Curtis, 354 F.3d 1347, 1358, 69 USPQ2d 1274, 1282 (Fed. Cir. 2004.

Response to Arguments

Applicants argue that the A3 position can include up to 12 amino acids and can be any naturally occurring amino acid. In a specific embodiment, applicants described the structure of the claimed peptides including that of the A3 position. Applicants have described that the A3 position can include up to 12 amino acids and can be any naturally occurring amino acid. In a specific embodiment, Applicants have demonstrated the preparation of a library of cyclic peptides comprising CX8C as well as XCTWX4LTCX, wherein X4 is any naturally occurring amino acid. See the specification at page 23, Example 1 and page 35, Example 5. Applicants have further described many specific embodiments at page 29 in the specification.

In reply, it is not controverted that page 29 recites ***specific*** embodiments having the core sequence of A3. What is controverted is the lack of written description for A3 comprising e.g., of 12-residue amino acid from the naturally occurring ones that can be combined to make up the A3 residues. The disclosure does not describe the numerous different combinations that can possibly result in combining naturally occurring residues. More importantly, whether the function of cyclic formation and beta turn is achieved with any combinations in the A3 residues. Furthermore, it is not clear how said

library can be isolated given no structure for the A3 position, except of course, the specifically isolated library with A3 having a defined residues.

Applicants argue that the disclosure have disclosed and exemplified a representative number of species within the claimed genus. One disclosure specifically exemplifies a scaffold shown to stabilize the turn EGNK (Example 1), the C'-C" hairpin loop (residues 37-46)of the CD4 region of HIV gp120 (Example 2), the turn sequence ENGK, the turn sequence QGSF the turn sequence KGNE; the turn sequence VWQL from the F-G loop of domain 2 of human Fc-epsilon-Rl (Example 2), and the turn sequence GPLT from the EPO agonist peptide EMPI (Example 2). Indeed, the specification discloses that some of these sequences are "difficult" turns yet were successfully stabilized by the claimed peptide scaffold (page 29, lines 10-12). Therefore Applicants submit that the specification discloses a representative number of species of the genus of A3.

In response, as acknowledged by applicants above, the specific sequence for A3 of defined structure is obtained from a known peptide having the known beta turn sequence. One skilled in the art would have known that these turns albeit, difficult would be expected since the amino acid sequences are derived from the known proteins with the known beta turn sequences.

(Specification at page 11, lines 24-29). However, the claims do not recite any protein from which the generic sequences have been obtained. Neither does the claims e.g., claim 1 recite that a beta turn for the sequence recited therein can result in any type of turns or would exhibit no turn for amino acid sequences of known defined structures for some of the given residues. There is no limitation in the claims as to the residue(s)that can provide this beta turn, as in claim 23. The specification recites that such beta turn can occur only for the known amino acids at the N or C terminus and not as the claimed 1-50 amino acids i.e., a long length polypeptide of at least 50 amino acids. Applicants submit that the Examples show that turn sequences are in fact stably presented in the claimed cyclic peptides. Applicants submit that the Examiner has provided no evidence that the presence of additional residues on either end of the claimed peptides would cause conformational instability.

In reply, the Examples show specific sequence with specific length. It is generally known that the conformational freedom that promotes binding, e.g., by modifying the peptides into the protein sequences, might be restricted which may likely perturb the function and stability of the protein in ways difficult to predict and measure. Some proteins accommodate insertions (variations) at numerous sites throughout their primary

sequence. Others are much less accommodating. It is difficult in general to predict which proteins are robust to insertions, and which sites in a particular protein are best suited to insertion of multiple independent sequences. The complex spatial configuration of amino acid side chains in proteins and the interrelationship of different side chains in the randomized sites are insufficiently understood to allow for such predictions. Selective (site-directed) mutagenesis and saturation mutagenesis are of limited utility for the study of protein structure and function in view of the enormous number of possible variations in complex proteins. There are still no rules that have emerged that allow structure to be related to sequence in any simple fashion (even as applied to the actual compounds).

(Incorporating the limitation of claim 11 to claim 11 would overcome this rejection].

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 23, as amended, is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to

particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 23, as amended is confusing in X1 and X2 has 1-50 amino acids. How can a library be isolated from an unidentified polypeptide containing residues?

Claim Rejections - 35 USC § 103

Claims 1-3, 7-10 and 20-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wrighton et al (5,830,851) for reasons advanced in the last Office action on 10/29/04 and 10/06/03.

Response to Arguments

Applicants argue that Wrighton et al does not disclose a library of peptides comprising W at the position corresponding to M and W or L at positions corresponding to A4 of the present claims. Rather, in the preferred embodiments, X5 of Wrighton et al., which corresponds to A2 of Applicants' claims, specifies M, F, or 1.

In reply, attention is drawn to Wrighton's disclosure of the different isolated specific peptides, for example, at position 2, as shown at ***e.g.,*** Table 7, col.3, Seq. ID 86 and 89 can be, inter alia, trp. The residue at position 1 can be Trp or H or A (corresponding to X4) that the various residues can have

any of the 20 naturally occurring residues at one position of the peptide sequence. Furthermore, with the definition of A3 as amino acid of 3-12 amino acid residues, the location designation for A4 becomes arbitrary. For example, if it is 12-residue then A4 becomes position A13 residue. One having ordinary skill in the art would expect the claimed combination given that each of the residues between the two Cys-Cys as any of the 20 natural residues. Furthermore, without the complete sequence it is not clear as to how the cyclic peptides present a secondary structure, such as beta-turn hairpin structure. See example claim 1. The specification teaches that the beta turn only occurs for a specific amino acids derived from a known protein wherein said turn already known to exists. Hence, since Wrigthton teaches a specific peptide sequence, it is considered that such turn would be inherent to the peptide of the defined sequence. It would be within the ordinary skill in the art at the time of the invention to determine turns given the sequence using known techniques at the time of the invention.

Applicants argue that Wrighton is concerned with solving a different problem than that of the applications. Wrighton does not teach or suggest the desirability of forming a trp-trp or trp-Leu cross-strand pair between A2 and A4 as a means of enhancing hairpin stability. Applicants argue that the failure

of Wrighton to teach any properties or uses of the disclosed peptides that are similar to those of the presently claimed peptides is evidence of nonobviousness.

In reply, not just because Wrighton does not expressly recite said property of a defined sequence does not make the claimed library non-obviousness. Applicants are, in effect, arguing that a compound (i.e., isolated library) suggested by the prior art, and hence, potentially in possession of the public, is patentable to them because it also possesses, an inherent, but hitherto unknown property, which they claim to have discovered. This is not the law. A patent on such a structure would remove the public that which is in the public domain by virtue of its inclusion in or obviousness from the prior art. In re Wiseman 201 USPQ 658. with to determine such stability property, as all peptide sequence ought to be, would be within the ordinary skill in the art at the time the invention was made. It is well known in the art that a peptide of a given primary structure assumes different turns e.g., beta for its stability.

Applicants argue that the claims are not limited to merely reciting the amino acid at position A2, but also recites that the amino acids at positions A1 and A5 are W, Y, F, H, V, T or

I. Applicants submit that the peptide sequence of Seq. ID. 89 or 86 are not a species falling with the present claims.

In response, this is a 103 rejection (not 102) hence; the species 86 or 89 does not fall within the claimed genus. What is essential is Wrighton's disclosure that the amino acid residues between the two Cys-Cys residues can be any of the 12 naturally occurring residues. Seq. ID. 86 or 89 is used to point out that position two between the cyclic peptide, Cys-Cys can be Trp, one of the 20 naturally occurring amino acids. The other peptide sequences e.g., Seq. ID. 84 discloses a Val at position A2. The claimed library even with the defined A1 and A2 residues, which are natural residues, would have been obvious in view of the teachings of Wrighton of an isolated library covering A1 and A2 which are included in the 20 natural amino acid. It would be within the ordinary skill in the art to arrive at the specific combination, as claimed.

Applicants argue the mere assertion in the prior art that a given position can be "any amino acid" does not provide a motivation to modify a peptide to a particular amino acid at that position. Merck is inapplicable since it revolved around combinations of compounds and not upon the modifications of those compounds. The prior art in Merck was directed to compositions comprising the combination of two compounds

selected from two classes of compounds known to be useful as diurectic. The holding in Merck merely states that the prior art rendered obvious claims directed to compositions comprising a specific compound from each of the classes of compounds disclosed by the prior art.

In reply, 20 naturally occurring amino acid is not "any amino acid". One having ordinary skill in the art would know what the 20 naturally occurring amino acids are. The instant specification also defines such naturally occurring amino acids. The claim is to a library i.e., a collection of compounds hence, the library of Wrighton wherein each of the positions X3, X4 and so forth forms a library. Wrighton discloses the numerous kinds of species obtained from the library containing in each positions 20 natural amino acids. This confirms to one having ordinary skill in the art that the presence of the 20 naturally occurring amino acids at these positions result in numerous possible combinations i.e., library. The rationale that it is "obvious to try" is not proper. The claimed library is obvious to do given the library of Wrighton each with a defined amino acid (20 natural amino acids) at the designated positions of the peptide sequence library. The isolation of the different species showing the utilization of each of the amino acids at the designated positions indicate the obviousness of the claimed

peptide library. The Merck holding is applicable herein since the compounds taught by Wrighton do not involve modifications. Rather, a specific teaching that defines a library with each of the X variables as one of the 20 naturally occurring amino acids. There is a multitude of effective combinations as taught and shown by Wrigton. Simply because applicants found one combination from the numerous combinations does not render the specific combination non-obvious. One having an ordinary skill in the art can arrive at the instant combination given the known 20 naturally occurring residues from which one can pick and choose.

Double Patenting

Claims 1-3, 7-12 and 20-23, as amended, are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5, 7, 9-11, 13 and 18-25 of copending Application No. 10/271,343 ('343 application).

Response to Arguments

Applicants will consider whether to file a terminal disclaimer, if appropriate, upon indication of allowable claims. In reply in the absence of a terminal disclaimer, the rejection is maintained.

Allowable Subject Matter

Claim 1 would be allowable if dependent claim 11 would be incorporated therein.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is(571)272-0812. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571)272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

T. D. Wessendorf
Primary Examiner
Art Unit 1639

Tdw
February 24, 2006